II. REMARKS

The undersigned attorney and firm have taken over representation of this application. Duly executed papers to this effect will be filed shortly. The Examiner is advised that the following documents will be forthcoming:

1. An Information Disclosure Statement and references cited therein;
2. Request to add an inventor to the present application including accompanying documents; and
3. Revocation of power of attorney and appointment of new power of attorney forms.

It is respectfully requested that the Examiner review all of the above-identified documents together with this amendment.

Claims 1, 4-34, and 37-51 are pending in this application. Claims 1 and 3-34 and 37 were previously presented, and claims 38-51 are new. By way of the foregoing Amendments to the Claims, claims 1, 19, and 37 have been rewritten in order to place those claims in condition for allowance . The subject matter of now–cancelled claim 3 has been incorporated into claim 1. Claims 35-36 have been canceled without prejudice. To expedite allowance, Applicants have focused claims 1, and 3-34 on a matrix comprising a homogenous mixture of an emulsion of an aqueous phase and an oil phase (i.e., an emulsion), in which the aqueous phase contains both the cross-linked polymer and the at least one therapeutic agent. Claim 37 has been amended to call for an emulsion of an aqueous phase and an oil phase, and at least one cross-linked polymer in said aqueous phase

A. The Rejections Under 35 U.S.C. Section 103(a)

In the Office Action dated April 17, 2003, the Examiner rejected claims 1 and 3-37 over Wallace et al. (U.S. Patent 6,312,725) in view of Grinstaff et al. (U.S. Patent 5,498,421). The Examiner asserted that Wallace et al. discloses a two-component polymer composition useful for drug delivery that when mixed together react to form a matrix at the site of administration, yet Wallace et al. does not specifically disclose an oil phase and thus does not provide the composition in the form of emulsions. The Examiner further took the position that Grinstaff et al. provides compositions for in vivo delivery of solid or liquid active agents contained in cross-linked polymeric shells, and that the active agent may be dispersed in oil and the polymeric shells containing the active agent may be suspended in an aqueous medium to form lipid-containing emulsions.

The Examiner asserted that it would have been obvious to modify Wallace et al.'s compositions by providing the composition in the form of an emulsion, as taught by Grinstaff et al. The Examiner went on to assert that because of Grinstaff et al's teaching that water-insoluble drugs can be dispersed in oil and included in polymeric shells suspended in an aqueous phase, that one of skilled in the art would have a reasonable expectation that the instant compositions and methods would be successful.

In the Section of the of the Office Action dated April 17, 2003 concerning the Examiner's Response to Arguments section (pages 4-5), the Examiner noted that the claims as presented at that time did not exclude the presence of polymeric shells, as described by Grinstaff et al., and that "the features upon which Applicant relies (i.e., crosslinking in the aqueous phase and the biophysical and biologic release properties of the oil phase, such as texture and elasticity)" were not recited in the rejected claims.

Applicants respectfully request reconsideration of the rejection in light of the amendments to previously rejected claims, which are believed to place them in condition for allowance. Applicants have focused the previously rejected claims in this application on a matrix which is an aqueous-oil emulsion with a cross-linked polymer and at least

one therapeutic agent in the aqueous phase. More particularly, claim 1 has been revised to more particularly define one embodiment of the invention, where the matrix comprises an emulsion of an aqueous phase and an oil phase," with the cross-linked polymer specified as being in the aqueous phase. With the rewriting of claim 1 to more clearly point out this embodiment of the invention, Applicants believe that the claimed invention is not obvious in light of the combination of Wallace et al. and Grinstaff et al.

Independent claim 19 is directed to a method of preparation. This claim has also been amended to state that an emulsion is prepared of an aqueous phase and an oil phase. The claim previously and currently states that the aqueous phase comprises a polymer.

Independent claim 37 has also been amended to call for an emulsion of an aqueous phase and an oil phase, with at least one cross-linked polymer in the aqueous phase.

As acknowledged by the Examiner, Wallace et al. has no disclosure of oil or an emulsion in its cross-linked aqueous (the only) phase. Grinstaff et al. is solely focused on polymeric shell-coated oil microparticles containing a therapeutic agent, the oil microparticles which may be suspended in or emulsified in an aqueous medium. If one were to utilize the polymer composition of Wallace et al. as the polymeric shell of Grinstaff, it is respectfully submitted that an emulsion of the aqueous phase and the oil phase would not result. It is respectfully submitted that the emulsions described in Grinstaff et al. would not comprise the polymeric composition nor the oil phase, as called for in amended claim 1 ("...said matrix comprising an emulsion of an aqueous phase and an oil phase..."); rather at best the combination would result in "particles of a biologic substantially completely contained within a polymeric shell, or associated therewith,...delivered neat, or optionally as a suspension in a biocompatible medium" (which can be a lipid-containing emulsion). See Grinstaff, et al. at column 9, lines 59-column 10, line 2. Moreover, the therapeutic agent would be a solid or optionally dispersed in a dispersing agent (which can be an oil; see, Grinstaff et al. at column 9, lines 23-46). The overall arrangement of phases in Grinstaff, et al. would not be changed by the use of the Wallace et al. polymer to form the polymer shell of Grinstaff, et al.

It is respectfully submitted that the arrangement of materials in Grinstaff, et al. do not disclose or suggest the arrangement set forth in independent claims 1, 19 and 37. In contrast, claim 1 calls for the " at least one therapeutic agent present in said aqueous phase, and at least one cross-linked polymer in said aqueous phase physically entrapping said at least one therapeutic agent." It is respectfully submitted that the combination proposed by the Examiner would be deficient at least because (i) there would still be no suggestion to prepare a matrix comprising the oil and aqueous phase emulsion called for in claim 1; (ii) the polymeric shell is not a matrix, nor could it be considered to be part of an emulsion.

Similarly, independent method claim 19 calls for the preparation of an emulsion in step i). An emulsion as presently claimed is simply never arrived at via the combination of the references relied upon by the Examiner, except as a medium for delivery of the polymer shells (described in Grinstaff, et al.). Even in that case, such an emulsion does not contain a matrix which is formed in step ii) of claim 19. Furthermore, the combination would never result in the therapeutic agent being entrapped in a matrix, as set forth in claim 19.

Independent claim 37, which as amended calls for an emulsion of an aqueous phase and an oil phase, with at least one cross-linked polymer in the aqueous phase, is also respectfully submitted to be patentable over the combination of Wallace, et al. and Grinstaff et al. because an emulsion of an aqueous phase comprising the cross-linked polymer and an oil phase is simply never arrived at via the combination of these references.

B. New Claims

New claims 38-49 have been added by virtue of this amendment. These claims are directed to an embodiment of controlled release compositions of the invention where the aqueous phase contains the cross-linked hydrogel polymer matrix, and the lipid phase is physically entrapped within said polymer matrix. The lipid phase includes at least one

therapeutically active agent contained therein. As stated in claim 38, the hydrogel polymer matrix provides a controlled release of said therapeutically active agent when the composition is administered to a bodily compartment of a mammal.

C. Support for the New Claims

New independent claim 38 is directed to a controlled release composition for administration of a therapeutic agent to a mammal, comprising an aqueous phase containing a cross-linked hydrogel polymer matrix, and a lipid phase physically entrapped within said polymer matrix, said lipid phase having at least one therapeutically active agent contained therein, said hydrogel polymer matrix providing a controlled release of said therapeutically active agent when the composition is administered to a bodily compartment of a mammal.

Support for the language of new claim 38 is found throughout the specification, and it is respectfully submitted that no new matter has been added. Specifically, support the aqueous phase containing the polymer is found, e.g., at page 4, lines 10-12 of the specification. The fact that the polymer may be cross-linked is found throughout the specification, e.g., at page 4, lines 5-8; and page 4 line 23 through page 5, line 10. The polymer being a hydrogel matrix is found throughout the specification, e.g., at page 10, line 19 through page 11, line 19. The possibility that the lipid phase may be entrapped within the polymer in the aqueous phase is found, e.g., at page 4, lines 6-10. The therapeutically active agent may be in the oil (lipid) phase, as set forth at page 4, lines 5-12. The fact that the composition is administered to a body compartment of a mammal is also clearly supported by the specification, see, e.g., page 5 lines 22-23 and original claims 25-26.

With respect to the new dependent claims, claim 39 is a combination of original claims 5 and 6; claim 40 is supported by original claim 7; claim 41 is supported by original claim 10; claim 42 is supported by original claim 11; claim 43 is supported by original claim 13; claim 44 is supported by original claim 14; claim 45 is supported by original claim 15; claim 46 is supported by original claim 16; claim 47 is supported

throughout the specification, and specifically at page 14, line 18 through page 15, line 1 of the specification; claim 48 is supported throughout the specification, and specifically at page 27, line 20 through page 28, line 20, and page 31 lines 8-11 of the specification; claim 49 is supported throughout the specification, and specifically at page 40, lines 14-23; claim 50 is supported by original claim 16 and throughout the specification, specifically at page 13, line 19 through page 14, line 7 of the specification (regarding a controlled rate of release in situ), and at page 13 line 1 and page 15, line 10 and original claim 28 (regarding diffusion of the therapeutically active agent from the matrix); and claim 51 is supported throughout the specification, and specifically at page 36, lines 20-22.

D. Patentability of the New Claims

It is respectfully submitted that Wallace, et al. and Grinstaff, et al., either alone or combined, do not anticipate claim 38 nor render it obvious. It is respectfully submitted that Wallace does not disclose or suggest a lipid phase. It is respectfully submitted Grinstaff, et al. does not disclose or suggest a hydrogel polymer matrix; instead it describes a polymer shell. In embodiments where the therapeutically active agent is contained in an oil phase within the polymer shell (see Grinstaff, et al. at column 9, lines 23-46), the therapeutically active agent would be *contained inside* the polymeric shell, and would not be physically entrapped *within* a hydrogel matrix, as called for in claim 38. In this regard, the Examiner's attention is further directed to the language of new dependent claim 50, which states that the therapeutically active agent *diffuses* out of the hydrogel polymer matrix in situ.

It is respectfully submitted that new claims 38-51 are each patentable over any combination of the art relied upon by the Examiner in the Office Action dated April 17, 2003.

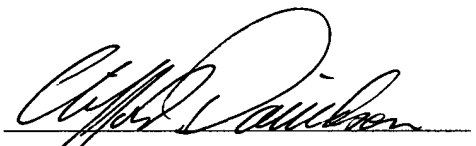
Furthermore, in view of the scope of the search previously performed by the Examiner, it is respectfully submitted that the consideration of new claims 38-50 would not present any burden at this time.

III. CONCLUSION

In view of the actions taken and arguments presented, it is respectfully submitted that reconsideration of the amended claims and withdrawal of the previous rejection is warranted. Furthermore, it is respectfully submitted that new claims 38-51 also patentably differentiate from the art relied upon by the Examiner, and should be considered and allowed at this time.

An early allowance is earnestly sought. Should a discussion aid in furthering the prosecution of this application, the Examiner is invited to telephone the undersigned at (212) 736-1940, ext. 101, to effect a resolution.

Respectfully submitted,
Davidson Davidson & Kappel, LLC

By: 

Clifford M. Davidson, Esq.
Attorney for Applicant(s)
Registration No. 32,728

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940